REMARKS

Claim 2 has been amended to more clearly identify the BabA protein.

Claim 3 has been amended to indicate that the immunoglobulin composition is isolated, monospecific, binds specifically to H-1 blood group antigen-glycoconjugates and is not a HopA, HopB, HopC, HopD or HopE protein. Support for these amendments can be found in the Specification on page 7, lines 16-19 and claim 2.

Claim 4 has been amended by deleting reference to fractions and preferred molecular weight ranges. The preferred ranges have been placed in newly added, dependent claims 27 and 28.

Claim 5 has been amended by deleting reference to fractions.

Claim 6 has been amended to indicate that the antibody is isolated, monospecific, binds specifically to H-1 blood group antigen-glycoconjugates and is not a HopA, HopB, HopC, HopD or HopE protein. Support for these amendments can be found in the Specification on page 7, lines 16-19 and claim 2.

Claim 7 has been amended by deleting reference to fractions and preferred molecular weight ranges. The preferred ranges have been placed in newly added, dependent claims 29 and 30.

Claim 8 has been amended by deleting reference to fractions.

Claim 16 has been amended by incorporating the subject matter of claims 17 and 18.

Claim 19 has been amended by incorporating the subject matter of claims 20 and 21.

No new matter has been added.

1. RESTRICTION REQUIREMENT

In the Office Action dated May 12, 2005, the Examiner acknowledged that the process claims that depend from and/or

include all of the limitations of the product claims will be rejoined when the product claims are found allowable.

2. NON-PATENTABLE SUBJECT MATTER

The Examiner has rejected claims 3-8 as being to non-patentable subject matter because they cover naturally occurring substances. Applicants have amended claims 3-8 to cover an "isolated" immunoglobulin composition or antibody, thereby overcoming the rejection.

3. DOUBLE-PATENTING

The Examiner has rejected claims 17-18 and claims 20-21 contending that the claims are substantial duplicates of claims 3 and 16, and 6 and 19, respectively.

Applicants have amended claim 16 to include the subject matter of claims 17 and 18. Claim 19 has likewise been amended to include the subject matter of claims 20 and 21. Thus Applicants respectively request reconsideration and removal of the rejection.

4. CLAIM REJECTIONS UNDER 35 USC §102

The Examiner has rejected all of the claims for lack of novelty over three references: Boren et al (1994), Durrant et al. (1993), and Alemohammad (U.S. Pat. No. 5,626,156).

4.1 NOVELTY REJECTIONS BASED ON BOREN ET AL., 1995

The Examiner states that the present invention is directed to colostrum that comprises polyclonal antibodies/immunoglobulin that will bind to a Lewis^b binding adhesion protein of *H. pylori*. The Examiner further states that Boren et al. disclose a human colostrum secretory IgA that specifically binds *H. pylori's* Lewis^b

antigen binding protein and successfully inhibits bacterial adherence to cells. The Examiner concludes that Boren's composition of human secretory IgA immunoglobulin anticipates the instant invention. Applicants respectfully traverse.

The Boren et al. publication reports experiments identifying the receptor on the surface of gastric mucosal cells to which *H. pylori* proteins bind in the process of attaching to gastric mucosal cells. Specifically, Boren et al. reports that pre-incubation of *H. pylori* with secretory IgA isolated from human colostrum inhibited subsequent binding by *H. pylori* to gastric mucosal cells. In contrast, the same pre-incubation experiment conducted with IgA antibodies isolated from serum failed to inhibit *H. pylori* binding to gastric mucosal cells (see pg 32). The conclusion drawn from this experiment is that the colostrum secretory IgA antibodies present the same attachment-mediating receptor to *H. pylori* that the gastric mucosal cells do.

The distinction between secretory IgA antibodies isolated from colustrum and IgA antibodies isolated from serum is that the colostrum secretory IgA antibodies are conjugated with carbohydrate whereas serum IgAs are not. Based on this distinction, Boren et al. ran experiments with monoclonal antibodies directed against carbohydrate antigens, specifically the Lewis^a and Lewis^b antigens. Only secretory IgA isolated from colostrum detected Lewis^a and Lewis^b antigens: the Lewis antigens were not detected by IgA antibodies from sera. The conclusion that Boren et al. draws from this result is that Lewis^a and Lewis^b carbohydrates are candidates for the receptor to which *H. pylori* binds to attach to gastric mucosal cells (see Boren et al. (1993) Science 262:1892-1895; attached).

Through additional experiments, Boren et al. identifies Lewis^b protein conjugates as potent inhibitors of *H. pylori* attachment to gastric mucosal cells, whereas Lewis^a protein conjugates do not have such inhibitory activity. The conclusion drawn here is that "Lewis^b antigen is an essential part of the cell surface H. pylori receptor" (see Boren and Falk, 1995, page 32). At no point does Boren et al. describe any antisera or antibody that binds to the adhesin protein via its hypervariable region. That is, the secretory IgA molecules do not specifically bind adhesin, rather adhesin specifically binds the fucosylated Lewis^b antigen presented on the secretory IgA molecule.

The instant application describes **monospecific** antisera and antibodies raised against BabA protein from *Helicobacter pylori* that specifically recognize and bind to BabA protein. Stated clearly, the Boren et al. publication does not anticipate the present invention because the Boren et al. antibodies bind to a carbohydrate antigen, the Lewis^b carbohydrate, whereas the antisera and antibodies of the present invention bind to protein antigen, the adhesin protein of *H. pylori*.

In view of the above, Applicants respectfully request reconsideration and removal of the rejection.

4.2 Novelty rejections based on Durrant et al., 1993

The Examiner states "Durrant et al. disclose a rat polyclonal antiserum that comprises purified immunoglobulin anti-idiotypic antibodies that evidence the Lewis^b antigen epitope confirmation, which would specifically bind to and form a complex with *Helicobacter pylori* Lewis^b antigen binding antigen as Durrant showed that the rat antiserum comprised anti-ID Lewis^b antigen presenting immunoglobulins." Applicants respectfully traverse.

As described above, the invention of the current application involves monospecific antisera and antibodies that specifically recognize a *Helicobacter pylori* attachment protein, BabA. The BabA protein, bound by the antibody of the present invention, binds to fucosylated blood group antigens such as Lewis^b. The Examiner alleges that the anti-idiotypic antibody produced from the antibody recognizing Lewis^b would mimic the Lewis^b antigen and thus bind BabA. But there is no guarantee that this will occur.

In the attached reference (Agius et al. (1988) Journal of Immunology 140:62-68), the authors study the interaction between an antigen and its anti-idiotypic antibody, and the antibody. The results indicate that the antigen and its anti-idiotypic antibody do not bind to overlapping sites on the antibody. As a consequence, the anti-idiotypic Lewis^b antibody would not necessarily bind BabA.

Furthermore, BabA is not an antibody against Lewis^b, but is simply a binding protein. Thus, it would seem that if there is no guarantee that an antigen and its anti-idiotypic antibody would both bind the antibody, then there is even less likelihood that an anti-idiotypic antibody, which may present some altered binding domain, would specifically bind with an unrelated molecule such as a binding protein.

Applicants also note that the claims have been amended to require that the BabA protein binds both Lewis^b and H-1 blood group antigen-glycoconjugates. This is missing from Durrant.

In view of the above, applicants respectfully request reconsideration and removal of the rejection.

4.3 Novelty rejections based on Alemohammad (U.S. 5,262,126)

The Examiner contends that Alemohammad disclose polyclonal immunoglobulin compositions/preparations purified from

Helicobactor pylori infected patient's serum and urine that specifically bind to *H. pylori* disease associated antigens. The Examiner states that the immunoglobulins specifically reacted with a plurality of antigens in the range of 31-66 kDa and inherently comprise the instantly claimed immunoglobulins. Applicants respectfully traverse.

Alemohammad describes a series of immuno reactive *H. pylori* proteins of varying molecular weights (see Fig 1, Fig 2, and Table 1). In this paper, antibodies from human sera and urine were used to probe immuno-blots in order to detect *H. pylori* proteins, and a series of H. *pylori* proteins of different molecular weights were identified. Importantly, **none** of the H. *pylori* protein bands detected by Alomohammad demonstrate the 70-77kDa molecular weight of the BabA protein described in the current application.

Applicants also point out that Alemohammad does not disclose a monospecific immunoglobulin composition or antibody, as is required by the instant claims.

Thus, Applicants respectfully request reconsideration and removal of the rejection.

5. CLAIM REJECTIONS UNDER 35 USC §103

The Examiner has rejected claim 2 as obvious over Alemohammad (U.S. Pat. No. 5,626,156) in view of Foster et al. (U.S. Pat. No. 4,444,879). The Examiner contends that Alemohammad teaches kits containing reagents to carry out diagnostic immunoassays with an immunoglobulin composition but failed to show the incorporation of anti-*Helicobacter pylori* protein human polyclonal immunoglobulin antisera into the kit.

The Examiner further contends that Foster et al. discloses positive and negative controls and a known standard specimen of Ig for quantitation. Based on these disclosures, the Examiner contends that it would have been obvious for a person skilled in the art to incorporate the immunoglobulin control of Forester et al. into the kits of Alemohammad to obtain the present invention. Applicants respectfully traverse.

As discussed above, Alemohammad does not disclose any proteins in the size range claimed by Applicants; 70-77 kDa, 73-75 kDa and, importantly, 73.5 kDa. The largest protein shown by Alemohammad is only 66 kDa. Additionally, Alemohammad indicates that other antigenic proteins are absent (see column 7, lines 28-31). This is not atypical because many proteins are destroyed or degraded during a particular type of purification scheme. Consequently, the skilled artisan would not be motivated to use Alemohammad, which does not contain the protein sizes desired and which teaches that not all antigen fractions are present, to obtain the monospecific immunoglobulin composition or antibody of the instant invention. Furthermore, the skilled artisan would not have a reasonable expectation of success in obtaining the desired protein fraction.

The Foster et al. patent describes the general principles for an immunoassay kit, which needs to present both positive and negative standards for reactivity and sensitivity. This is a feature all immunoassay kits utilize and does not provide any teaching that would motivate the skilled artisan to use Alemohammad to obtain the desired protein fraction or to have a reasonable expectation of success in doing so.

In view of the above, Applicants respectfully request reconsideration and removal of the rejections.

Applicants submit that the present amendment places all of the claims remaining in the case, including newly added claims, as defining non-obvious, patentable subject matter. Reconsideration of the rejections and allowance of the claims are respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is requested to contact Susan W. Gorman (Reg. No. 47,640) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursant to the provisions of 37 C.F.R §§ 1.17 and 1.136(a), Applicants petition for an extension of three (3) months to November 12, 2005 for the period in which to file a response to the Office Action dated May 12, 2005. The Commissioner is authorized to charge Deposit Account No. 02-2448 in the amount of $510.00 for this extension of time fee.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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0825-0176P

By _____

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Attachments: PTO 1449
References

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope to: Commissioner for Patents, P.O. Box [illegible], Alexandria, VA 22313-1450, on: 11/14/05 (Date of Deposit)

BIRCH, STEWART, KOLASCH & BIRCH, LLP

(Signature)

Nov. 14, 2005 (Date of Signature)